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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1632	4

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/230,195	RYBAK ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on th c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-35,37,38 and 40-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-35,41 and 42* is/are rejected.

7)☒ Claim(s) *37,38 and 40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' amendment filed 7-22-03 has been entered. Claims 2, 34, 41 and 42 have been amended. Claims 1, 2, 4-35, 37, 38 and 40-42 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 2, 4-35, 41 and 42 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention and is repeated for the reasons set forth in the preceding Official action mailed 1-17-03 (Paper No. 18). Applicant's arguments filed 7-22-03 have been fully considered but they are not persuasive.

Applicants argue that the claimed composition are transduction vectors for introducing genes into a cell in vitro or in vivo, the rev sequences are introduced into the cell to control viral inhibitor sequences, and the specification teaches the component of the vectors and how to make and use the vectors. Applicants further argue that only one credible assertion of specific utility is needed for the claimed invention to satisfy 35 U.S.C. 101 and 35 U.S.C. 112 (amendment, p. 10, 11). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-17-03 (Paper No. 18). This is a 35 U.S.C. 112 first paragraph enablement rejection but not a 35 U.S.C. 101 rejection and one credible assertion of specific utility for the claimed

invention is irrelevant to the present rejection. The specification of the present invention must provide sufficient enabling disclosure for the claimed invention.

As discussed in the preceding Official action mailed 1-17-03 (Paper No. 18), the specification states "This invention relates to vectors for gene transfer and gene therapy, inhibition of viral and cancer cells by delivery of RNAs, recombinant cells and nucleic acids and the likes" (specification, p. 1 lines 11-13). The sole use of the claimed vectors as disclosed in the specification is for gene delivery and gene therapy. Thus, claims read on gene delivery or gene therapy *in vivo* in light of the specification. The specification only discloses inhibition of HIV replication by the combined expression of a Gag dominant negative mutant and EDN by transducing CEM cells with a tightly-controlled HIV-1 inducible vector *in vitro* and the anti-HIV activity of EDN in CEM cells as well as Jurkat cells *in vitro*.

The state of the art for gene therapy was unpredictable at the time of the invention as discussed in the cited references Deonarain, Verma, Eck, and Gorecki. The Achilles heel of gene therapy is poor efficiency of gene delivery. Although methods of making vectors were known in the art, however, the specification fails to provide adequate guidance and evidence for how to use the claimed HIV vector for gene delivery or gene therapy via various administration routes *in vivo* so as to provide therapeutic effect for a particular viral disease in a subject. The specification also fails to point out the correlation between the viral inhibitor encoded by the claimed vector and a particular viral disease such that the expression of said viral inhibitor *in vivo* could provide therapeutic effect for said particular viral disease.

The fate of the DNA vector itself, the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking

of the genetic material within cellular organelles, and the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, the protein's compartmentalization within the cell, and the administration routes are all important factors for a successful gene therapy. Thus, one skilled in the art at the time of the invention would not know how to use the claimed vectors expressing various viral inhibitors for gene delivery or gene therapy via any administration route*s in vivo* so as to provide therapeutic effect for a particular disease or disorder in a subject. One skilled in the art at the time of the invention would have required undue experimentation to practice over the full scope of the invention claimed.

Applicants argue that the vector can be used with a pharmaceutical exipient for transducing cells in vitro or gene therapy in vivo (amendment, p. 11). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-17-03 (Paper No. 18) and the reasons set forth above.

Applicants argue that the specification teaches that the SD and SA subsequences contained within the vectors are functional (amendment, p. 11). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-17-03 (Paper No. 18). The specification defines "subsequence" as a region of the nucleic acid equal to or smaller than the specified nucleic acid (specification, p. 12, lines 7-9). The consensus sequence for SA is (U/C).sub.nN(C/U)AG*G and the consensus sequence for SD is (C/A)AG*GU where * represents the splice site. It was known in the art that AG*G or AG*GU are essential part of SA and SD, respectively. The claimed SA or SD subsequence encompasses any sequence that is smaller than the consensus sequence of SA or SD. However, the specification only indicates that

the SD and SA subsequences are functional but fails to provide adequate guidance and evidence that any SA or SD subsequence having nucleotide sequence lacking AG*G or AG*GU would still function as SA site or SD site for splicing. Thus, the specification fails to provide sufficient enabling disclosure for the full scope of the claimed SD or SA subsequence. Therefore, the claims remain rejected under 35 U.S.C. 112 first paragraph.

Conclusion

Claims 1, 2, 4-35, 41 and 42 are rejected. Claims 37, 38 and 40 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.